IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Chatterjee, D.K.

Appl. No. 09/558,421

Filed: April 26, 2000

For: **Mutant DNA Polymerases and Uses Thereof**

Art Unit: 1652

Examiner: Rao, M.

Atty. Docket: 0942.3600003/RWE/BJD

Declaration of Adam Goldstein

Honorable Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

I, Adam Goldstein, do hereby declare and say:

1. THAT, I, Adam Goldstein, hold the degree of B.S./M.S. A recent copy of my Curriculum Vitae, accurately listing my scientific credentials and work experience, is attached hereto as Exhibit A.

2. THAT, since September 15, 2001, I have been employed by Biogen. Prior to my current position, from 1990 to 1996, I was employed by Life Technologies, Inc. (LTI) (and now Invitrogen Corporation)[1], the assignee of the above-captioned application, in the capacity of Research Associate. *See* Exhibit A.

---

[1]Life Technologies, Inc. merged with Invitrogen Corporation on September 12, 2000, with Invitrogen Corporation being the surviving entity.

3. THAT, during my employment by LTI (and now Invitrogen Corporation), I worked under the supervision of Dr. Deb K. Chatterjee on a project involving the cloning, expression, and characterization of wild-type and mutant DNA polymerases.

4. THAT, I have reviewed my laboratory notebooks detailing my work on the project. Based on these laboratory notebook records and my recollection, the following activities involving my work, and relating to the DNA polymerase project, took place during the period from prior to October 17, 1994, until about September 8, 1995.

On or about September 6, 1994, bacterial cultures transformed with a plasmid encoding the mutant *Taq* DNA polymerase and cultured in the presence of IPTG to induce expression of the mutant *Taq* polymerase were given to me by Deb K. Chatterjee to assay for heat stable DNA polymerase activity. This mutant was expressed and found to have heat stable DNA polymerase activity. This experiment was recorded on page 90 of notebook 3865. A copy thereof is attached as Exhibit 1.

At the time the experiment described in Exhibit 1 was performed, I was supervised in my work relating to the cloning and expression of thermostable DNA polymerase by Deb K. Chatterjee, and had contact or discussions with Deb K. Chatterjee nearly every day regarding this project. Therefore, I believe the results of this experiment were communicated to by me to Deb K. Chatterjee soon after they were obtained and before October 17, 1994.

On or about December 5-7, 1994, I conducted experiments to prepare a purified preparation of the F667Y mutant of *Taq* polymerase. In this experiment, I lysed cells containing the mutant protein, performed PEI and ammonium sulfate precipitations on the lysate, and dialyzed the pellet. The polymerase was further purified on a heparin column. This experiment was recorded on page 100 of notebook 3865. A copy thereof is attached as Exhibit 2.

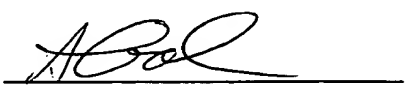
On or about December 10, 1994, I continued my experiment to prepare a purified preparation of the F667Y mutant of *Taq* polymerase. I analyzed data from the heparin column and assayed fractions from this column for polymerase activity. The fractions containing activity were pooled and dialyzed. This experiment was recorded on page 101 of notebook 3865. A copy thereof is attached as Exhibit 3.

6. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or document or any registration resulting therefrom.

Further, declarant sayeth not.

Date: 2/NOV 01

Name: Adam Goldstein

Signature: 

P:\USERS\BRIAND\0942\3600003\goldstein.declarn.wpd
SKGF1/25/98 dcw

Adam Stuart Goldstein

576 Kitty Street
Newbury Park, Ca 91320
mailto:zofob@aol.com

(805)-375 7797 (home)
(805)-375 6767 (work)

Exhibit A
Appl. No. 09/558,421

Summary: Technical Manager with 13 years industrial experience in the Biotechnology industry. Accomplished in new product and process development, product business development, and Operations management. Seeking a challenging position in a technical leadership or business development role for a progressive biotechnology or biopharmaceutical firm. I am seeking a position with company that has a clear vision for the future.

Professional Experience:

Baxter, Hyland –Immuno, Thousand Oaks, Ca **Jan. 2000 – Present**

Manufacturing Supervisor, Protein Purification

Review of GMP MBR's, Deviations, Actions and Alerts.
Staffing of Manufacturing Associates, training, H.R. reviews.
Implementation and review of OQ, and PQ documentation for Downstream.
Maintain Schedules and Run logs, assure adequate coverage for shifts; Day, Swing and Graveyard.

- Played key role in obtaining FDA, Canadian and EU licensure by federal agencies.
- Staffed and opened 2 new suites for Baxter site.
- Trained personnel in GMP's and FDA regulations.

GenVec Inc., Gaithersburg, MD **June.1998 – Jan. 2000**

Senior Process Development Scientist

Implemented GMP strategy to bridge R+D and P.D. scale for Downstream processing of Adenovirus vector.
Designed protein purification labs for the following:
GenVec's Process Development lab.
Contract Manufacturer flow of material.
Commercial Manufacturing Site, including cGMP personnel flows and HVAC.

- Implementation of purification using lab and commercial scale equipment, including Pharmacia skid.
- Perform viral particle analysis including HPLC assays, ELISA and SDS-PAGE analysis.
- Determine yields, Scale and optimize chromatographic steps.
- Responsible for transition of product from GenVec to contract manufacturer and transition to commercial manufacturing site.
- Implement and optimize downstream processing and coordinate plan to develop cell line contaminant assays.

KIRKEGAARD & PERRY LABORATORIES, Gaithersburg , MD **1996-1998**

Manufacturing / Process Improvement Manager

Accountable for technical and business development activities for custom product design and manufacture. Analyzed custom market needs, developed strategic initiatives, directed technical feasibility studies and coordinated the manufacture and distribution of customized products.

- Increased custom-based revenues over 1997
- Established new protein purification platforms in Manufacturing
- Substantial client interaction and development of business opportunities
- Developed quick screens for monoclonal and polyclonal assays. Responsible for scheduling of production runs, and assigning resources to projects. Reviewed protocols. Liaison to R&D, Q.C. and Document Control. Designed and implemented major process improvements which lead to substantial improvement in product quality, while reducing both lead times and costs.
- Principal resource for purification development and ISO 9000.
- Integrated operations units while improving service level, for both FDA and non regulated product lines.
- Developed and maintained a department budget. Created BOM's and captured true cost of product to new MRP system.

LIFE TECHNOLOGIES,INC., Rockville, MD **1990 –1996**

R&D Scientist

Assisted in activities for cost reduction, measurement improvement, statistical process control, capital projects, new revenue generation, automation, emergency production assistance, technical training and Manufacturing back-integration. Developed and transferred processes and product to manufacturing. Developed large-scale purification procedures for production. Developed assays for evaluation of purified proteins.

- Substantial cost reductions- approaching $2.5 million annualized savings
- Department introduced several new process technologies, and intellectual property, including a broadly applicable chemical cell disruption method, and broad implementation of tangential flow filtration (TFF)
- Isolation, purification, and testing of Modifying Enymes.
- Knowledge of DNA and RNA polymerases, nucleases, and other DNA enzymes.
- Developed purification schemes for the following: Taq DNA polymerase, Superscript-2, DNA gyrase, Hpa2, Thermatoga Neopolitina, reverse transcriptase and several more restriction enzymes from both native and cloned raw materials.

Masters, Biomedical Sciences/Molecular Biology, Hood College, Frederick, MD **1996**
Dissertation: "Purification and Characterization or rTEV Protease". Conducted novel independent research, and completed all requirements for a degree Biochemistry. Significant teaching/ tutoring load

Biochemical RegulatoryEngineering certificate, cGMP practices University of MD. **1997-1999**

B.S., Biology, Old Dominion University. Norfolk VA **1988**

CONTINUING EDUCATION AND TRAINING

Zenger Miler Leadership Training, Frederick, MD 1997

FDA workshops, Gaithersburg, MD 1997, 1998

Preparation for FDA audits, Gaithersburg, MD 1997, 1998, 1999

Trainer for Both Waters and Perceptive chromatography skids 1995-1998

Awards and Patents

- Special Recognition, cGMP Capability Installation (2000)
- Life Technologies Level III Award (1995)
- Life Technologies Level III Award (1996)
- Outstanding Contribution award (1997)
- U.S. Patent No. 5,861,295 (1999), Method for production of Nucleic Acid free Thermostable Enzymes.(Goldstein,Adam

PUBLICATIONS

Deborah A. Polayes and Adam S. Goldstein.: "Efficient Protein Expression and Simple Purification Using pProEX-1TM System" (1994)*FOCUS* vol.16 No.3 pp.81-84.

Deborah A. Polayes and Adam S. Goldstein.: "TEV Protease, Recombinant: A Site-Specific Protease for Efficient Cleavage of Affinity Tags From Expressed Proteins" (1994) *FOCUS* vol. 16 No.1, pp. 2-5.

ABSTRACTS

Goldstein, A.S., 1997. A Novel Method To Extract Proteins From Native or Cloned Organisms Using Noninvasive Procedures to Reduce Nonspecific Contamination by DNA and Junk Proteins. Prep-Tech'97.

Polayes, D.A., Goldstein, A.S., Efficient Release of Proteins and Peptides from Fusion Proteins by TEV Protease, Recombinant. ASBMB 1997.

Professional Organizations
American Society for Microbiology
American Chemical Society

Civic Organizations:
Condor Flying Club, Inc. (Cofounder)

Skills Summary: Technical Management, Project Management, Customer/ Client Interaction, Product and Process Development, Interpersonal and Team skills, Technical acumen and aptitude, tremendous work ethic, manufacturing systems; tremendous technical and analytical skills. Teaching, training and mentoring experience